

Message

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Sent: 6/28/2011 1:12:23 PM
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Subject: NEWS UPDATES: EPA Weighs Industry Methanol Studies, Opening Door To Weaker Risk Value (Risk Policy Report)

EPA Weighs Industry Methanol Studies, Opening Door To Weaker Risk Value

Posted: June 27, 2011

EPA is expanding its assessment of methanol's non-cancer risks to consider the results of several industry-backed studies that raise questions about the agency's extrapolation of risk data from mice to humans, a move that could open the door to EPA softening its proposed safety estimates for the substance.

In a June 22 *Federal Register* notice, EPA unveiled an addendum to its pending assessment that adds four additional studies -- including three sought by industry -- to the body of research that a panel of peer reviewers will consider prior to making recommendations on how officials should move forward with its Integrated Risk Information System (IRIS) non-cancer risk assessment for methanol. The agency will take comment on the new studies through July 6 before a contractor peer review workshop July 22.

Publication of the addendum marks a compromise with industry; bringing into the review studies that the sector's trade association and others argued were vital to creating an accurate safety estimates, but falling short of delaying the assessment's release, which industry had pushed for at May 26 EPA listening session, and updating the safety estimates to more accurately reflect high background levels of the substance.

At the time, agency officials said they were reviewing the industry studies, but were unclear on whether the information would be included in the presentation to the peer review panel (*Risk Policy Report*, May 27).

Industry supports the move, with one source saying "we are grateful to the EPA for putting out this addendum" and making the research available to peer reviewers. But the source continues, there are

other concerns with EPA's draft assessment -- namely a failure by the agency to take into account background levels of methanol when setting risk limits -- and the addendum only "addresses some of it."

Methanol is a chemical widely used in the production of alternative and renewable fuels, paints, plastics, solvents and textiles. EPA says it anticipates increased demand for methanol, especially in biodiesel production, although the agency says the need is "growing steadily in almost all end uses." EPA in its draft "Toxicological Review of Methanol (Non-Cancer)," released in March, sets a reference dose (RfD), or safe daily dose for ingestion, of 0.4 mg/kg-day, and a first-time reference concentration (RfC), or safe daily dose for inhalation exposure, of 2 mg/m³, levels industry says are far too conservative. When final, the assessment will update risk estimates that EPA completed in 1988 and will form the basis for a host of regulatory decisions.

The release of the draft assessment comes after almost a year of delay as agency officials grappled with how to handle data from a controversial Italian lab that was the basis of its cancer risk assessment for the substance. Industry protested the use of the Ramazzini Institute data, arguing that its protocol was unconventional and overstated cancer risk, leading EPA to calculate an overly stringent assessment of the chemical's cancer risks.

Following a review last spring of a selection of the Ramazzini lab's methanol slides by National Toxicology Program (NTP) pathologists, EPA pulled two finalized Integrated Risk Information System assessments and paused four pending assessments -- including methanol's -- while it considered how to handle the NTP finding that the lab may have been overstating risks.

NTP is expected to release its findings from a review of the Ramazzini data by the end of the month, according to the source, who adds that "we're really not hearing much" about what the findings will entail. The report is expected to assess five different Ramazzini studies, including those of methanol and the fuel additives ETBE and MTBE.

But while the agency awaits the review of the cancer data, it is moving forward on the non-cancer portion of the methanol assessment.

In the recently released addendum, the agency seeks to address complaints from industry that EPA failed to take into account more recent data developed since the release of the draft IRIS assessment in 2010.

Those more recent studies found that methanol metabolizes differently in primates and rabbits than in mice, which EPA relied on when proposing its RfD and RfC. For example, in June 17 comments on the draft review, Greg Dolan, director of the Methanol Institute (MI), an industry group, noted that the agency's draft document ignored recent research that "shows that either the rodent development effects from methanol exposure are irrelevant to human risk, or at the very least, humans are much less susceptible to development effects from methanol exposure than rodents."

Dolan pointed to recent industry funded studies by Canadian professor Peter Wells that "demonstrated that the metabolism of methanol in rabbits more closely resembles that of primates (measured in monkeys) than metabolism in rodents (mice)." What's more, Dolan continued, studies have further shown that different strains of mice and other rodents metabolize methanol differently making them an unreliable source of data. *Relevant documents are available on InsideEPA.com. (Doc ID: 2368215)*

In particular, Dolan notes three studies that Wells participated in, finding that rodents are not a good model for effects in humans because rodents are more sensitive to methanol; tests on rabbits are much more accurate because rabbits metabolize the substance in ways similar to humans; and there are differences between methanol's effects on rodents versus its effects on humans.

Kimberly Wise, a toxicologist for the American Petroleum Institute (API), reached similar conclusions in her June 6 comments, pointing to the three studies noted by MI and two others showing "that methanol metabolism in rodents is different from primates and rabbits. The publications call into question EPA's approach of using data from rodent studies to propose reference concentrations for human exposure."

Given these findings, Dolan continued, "EPA's assessment and its recommended reference levels therefore must be significantly altered to take these new research results into account."

EPA included three of the five studies MI and API pointed to in their comments and added a fourth by many of the same researchers.

While the inclusion of the new data for the review will help with correcting some of the inaccuracies in the document, the industry source says, the agency still "does not address the other issue of how EPA assesses the background levels of methane," which is the other issue industry brought up in comments.

Methane can be found in many foods -- most notably fruit juice, wine and beer -- but "We think that the EPA is assuming levels from the dietary exposure that are well below" the amount of methane currently present in most diets, the source says. "They made an assumption, particularly with the key modeling that was done, that they did not need to consider background levels and we don't think that's appropriate."

In particular, as Dolan wrote in the MI comments, "EPA's choice of such a low reference level suggests, by implication, that perhaps half or more of the population is at risk from their own background level of methanol."

What's more, in setting the very conservative background levels for methanol, EPA is repeating a mistake it made when doing its IRIS assessment for formaldehyde, a move that came under scrutiny in a recent National Academy of Sciences review that found "EPA was sort of discounting the role of background levels," the source says.

The source adds that industry hopes to discuss EPA's determined background levels for methanol with agency officials prior to the finalization of the document, and is "hopeful the issue can be resolved." -- *Jenny Hopkinson*

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